

REMARKS

The preceding claim amendments and the following remarks are submitted as a full and complete response to the Office Action issued on October 23, 2009. Claim 21 has been amended to recite that the denaturing buffer used in step (b) contains cysteine. Support for this amendment can be found throughout the specification, for example, at page 7, lines 7-8, and pages 15-16. Other amendments made in claim 21 are to incorporate the subject matter of the original claims 1, 2 and 17. Claims 22 and 23 have been added. Support for these new claims can be found, for example, in the original claim 7, Sequence Listing and Examples at pages 14-17. No new matter has been added by these claim amendments. Accordingly, claims 21-23 are pending. Reconsideration of all outstanding rejections is respectfully requested in view of the foregoing amendments and following remarks.

Rejection under 35 U.S.C. §112, first paragraph

The Patent Office has rejected claim 21 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Applicants respectfully traverse this rejection.

At the outset, Applicants note that claim 21 has been amended to recite the subject matter of the original claims 1, 2 and 17 in the present application and to further recite that the denaturing agent in step b) comprises cysteine. The amendments of claim 21 are fully supported by the original claims and the specification as originally filed, for example, the original claims 1, 2 and 17 and pages 7 and 15-16 of the specification.

Thus, Applicants respectfully submit that the amended claim 21 was fully described in the present application as originally filed¹. Therefore, one skilled in the art would readily understand that Applicants were in possession of the subject matter of the amended claim 21 at the time the present application was filed. Reconsideration and withdrawal of this rejection are respectfully requested.

Rejections under 35 U.S.C. § 103(a)

The Patent Office has rejected claim 21 under 35 U.S.C. § 103(a) as obvious over Andou et al. (U.S. Patent No. 6,551,801)(“Andou I”) in view of Hötten et al. (U.S. Patent No. 6,972,321)(“Hötten”). The Patent Office has rejected claim 21 under 35 U.S.C. § 103(a) as obvious over Andou et al. (WO 98/29559)(“Andou II”) in view of Hygene AG (EPO 1074620)(“Hygene”). Applicants understand that Andou I and II have been cited as a reference disclosing purification of dimeric BMP proteins including MP52 and that Hötten and Hygene have been cited as a reference disclosing producing monomeric BMP proteins including MP52 having a cysteine mutated to prevent intermolecular disulfide bonds. The Patent Office argues that it would have been obvious to purify the mutated proteins of Hötten or Hygene using the purification method of Andou I or II. Applicants respectfully traverse these rejections.

The amended claim 21 is directed to a process for producing a purified refolded monomeric MP52. While Andou I and II disclose a purification method for dimeric MP52, it is silent as to whether the same purification method can be also used in purifying monomeric MP52. Applicants respectfully submit that one skilled in the art would not

¹ The present application as referred to in this response does not encompass the parent applications.

have understood that the purification method and its results as disclosed in Andou I and II, which exclusively concern the dimeric protein, can necessarily be transferred to purifying monomeric MP52 according to the claimed method.

While Hötten discloses a purification method for monomeric MP52, as indicated in the Office Action at page 3, the purification method disclosed in Hötten is different and is distinguished from the currently claimed method. See page 3 of the Office Action.

The amended claim 21 is further distinguished from the purification methods disclosed in Andou I and II (for dimeric MP52) and Hötten (for monomeric MP52) since the denaturing buffer used in step b) of the claimed method contains cysteine. The purification methods disclosed in all of these cited references use a denaturing buffer (or a solubilizing buffer in Andou I and II). However, none of the denaturing buffers used in these purification methods contains cysteine. These cited references, thus, fail to teach or suggest using cysteine in a denaturing buffer for purification of MP52, let alone for purification of monomeric MP52.

Instead, the purification method disclosed in Andou I and II uses cysteine in a refolding solution. One skilled in the art would have readily understood that the denaturing buffer and the refolding solution perform opposite functions. That is, while the former destroys the secondary and tertiary structures of monomeric MP52, the latter restores them. Thus, in view of the opposite function of the denaturing buffer and the refolding solution, one skilled in the art would not have been motivated to use cysteine in the denaturing buffer in the claimed method from the teaching of Andou I or II that cysteine was used in the refolding solution, with reasonable expectation of success. This conclusion is further supported by the fact that the purification method for dimeric

MP52 disclosed in the present application also does not use cysteine in a denaturing buffer while a refolding solution contains cysteine. See Example, page 13.

Moreover, a mere combination of teachings of (1) Andou I and Hötten or (2) Andou II and Hygene would not have resulted in the claimed method because none of these cited references teaches or suggests using cysteine in a denaturing buffer or a solubilizing solution.

To establish a *prima facie* case of obviousness, all the claim features must be taught or suggested by the prior art. See *In re Royka*, 180 USPQ 580 (CCPA 1974). Since the cited references, alone or in combination, fails to teach or suggest all the elements of the amended claim 21, there is no *prima facie* case of obviousness established. Therefore, Applicants respectfully request reconsideration and withdrawal of these obviousness rejections.

In light of the foregoing, Applicants submit that all outstanding rejections have been overcome, and the instant application is in condition for allowance. Thus, Applicants respectfully request early allowance of the instant application. The Commissioner is hereby authorized to charge any fees or credit any overpayment to Deposit Account No. 02-2135.

Respectfully submitted,

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